

## Cigarette Smoking and Mortality<sup>1</sup>

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**Methods.** The relationship of cigarette smoking and smoking cessation to mortality was investigated among men screened for and also among those randomized to the Multiple Risk Factor Intervention Trial (MRFIT).

**Results.** Among the 361,662 men screened for the MRFIT, cigarette smoking was an important risk factor for all-cause, coronary heart disease (CHD), stroke, and cancer mortality. These risks, on the log relative scale, were strongest for cancers of the lung, mouth, and larynx. The excess risk associated with cigarette smoking was greatest for death from CHD. Overall, approximately one-half of all deaths were associated with cigarette smoking. Among the 12,866 randomized participants, weak positive associations with duration of cigarette smoking habit and tar and nicotine levels were found with all-cause mortality. For both SI and UC men, substantial differences in subsequent CHD (34-49%) and all-cause (35-47%) mortality were evident for men who reported cigarette smoking cessation by the end of the trial compared with those continuing to smoke. There was no evidence that lung cancer death rates were lower among cigarette smokers who quit compared with those who continued to smoke in this 10-year follow-up period.

**Conclusion.** The data are consistent with results of previous epidemiologic studies indicating that the benefits of smoking cessation on CHD are rapid, while for lung cancer, the benefit is not evident in a 10-year follow-up period. © 1991 Academic Press, Inc.

## INTRODUCTION

Major prospective studies completed in the 1960s and 1970s contributed substantially to our understanding of the relationship between smoking and disease (1). These studies provided estimates of relative and attributable risk associated with cigarette smoking. Relative risks for smokers compared with nonsmokers were greater for smoking-related cancers and chronic obstructive pulmonary disease than for coronary heart disease (CHD); however, of these smoking-related diseases, mortality due to CHD accounted for over one-third of the excess deaths due to cigarette smoking.

Since the 1960s, there have been relatively few longitudinal studies that have measured the effects of cigarette smoking on health. Most studies have had rel-

atively small sample sizes and have focused primarily on cardiovascular disease (CVD) endpoints, such as CHD or stroke. At the present time, there are only four large longitudinal studies in the United States that are evaluating the effects of smoking on a variety of disease endpoints: the Nurses' Health Study (2), the follow-up of the participants in the National Health and Nutrition Examination Survey (3), the American Cancer Society's volunteer study (4), and the follow-up of men screened for the Multiple Risk Factor Intervention Trial (MRFIT) (5,6).

### Previously Reported Results for 361,662 Men Screened for the MRFIT

Prior reports based on the men screened for the MRFIT have noted:

- (a) A clear dose relationship between cigarette smoking and both CHD and total mortality after 5 years among black and white men (6). The relationship between smoking and CHD mortality was stronger for the younger (35 to 44 years) than for older age (55 to 57 years) groups on the log relative scale but excess risk attributable to smoking was greater in the older age group (8).
- (b) A significant association between cigarette smoking and stroke (6, 9).
- (c) An increased risk of CHD mortality among diabetics who smoked cigarettes compared with nonsmoking diabetics (10).
- (d) A strong association between cigarette smoking and mortality due to chronic obstructive pulmonary disease (11).
- (e) The additive effects of smoking, cholesterol level, and blood pressure on CHD mortality (6).

### Previously Reported Results for 12,866 Randomized Participants

Prior reports for randomized participants have also indicated a strong relationship among cigarette smoking, CHD, total mortality, and incident myocardial infarction (12, 13). There was also a clear and striking dose-response relationship between the number of cigarettes smoked and lung cancer mortality (14). Cigarette smokers had decreased forced expiratory volume at 1 sec (FEV<sub>1</sub>) at entry to the trial and a greater decline in the FEV<sub>1</sub> over time as compared with former smokers or those who had never smoked (15). Decreased pulmonary function was also associated with increased cancer mortality among smokers (14). Low levels of beta-carotene or carotene in serum among cigarette smokers was an independent predictor of lung cancer (16).

Results from the first 7 years of follow-up in the MRFIT showed that while there was no difference in total mortality between the SI and UC participants, SI men experienced a 7% lower CHD death rate than UC men (5). After 10.5 years of follow-up, mortality rates were lower for SI men than UC men by 10.6% for CHD and by 7.7% for all causes (17). Men who had quit smoking in both the SI and UC groups had lower CHD and total mortality and a reduced incidence of nonfatal coronary events after 7 years' of follow-up compared with those who continued to smoke (5, 12).

The purpose of the current investigation is threefold: (a) to study the relationship of cigarette smoking with total and cause-specific mortality in the large cohort of men screened for MRFIT in the 1970s, thus providing updated information on the risks of cigarette smoking; (b) to examine the relationship between mor-

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ality and the tar and nicotine content of cigarettes smoked by the men randomized to MRFIT; and (c) to compare the mortality experience of men who quit smoking with that of those who did not.

### METHODS

Participants were selected for the trial from among 361,662 men age 35–57 years screened in 22 clinical centers in the United States, based on a combination of their cigarette smoking habits, diastolic blood pressure (DBP), and serum cholesterol levels at screen 1. A risk score was calculated using a logistic regression function derived from Framingham men in the same age group (18). Initially, men in the upper 15% and subsequently those in the upper 10% of risk were selected. Detailed descriptions of selection criteria data collected at the three screening visits (screen 1, screen 2, and screen 3) and intervention results are given elsewhere (5, 19–21).

Proportional hazards regression models were used to evaluate the association between cigarette smoking and subsequent mortality (22) and to compare mortality rates for the SI and UC groups. Measures of smoking dose were divided into three or more categories and adjusted relative risks were estimated for each category relative to the first. In addition, analyses which treated measures of smoking dose as continuous variables and which compared all smokers versus nonsmokers were also performed. Baseline covariates included in regression models are footnoted in the tables. Cause-specific mortality was based on death certificates coded by trained nosologists using the Ninth Revision of the International Classification of Diseases (23).

### RESULTS

#### Men Screened for MRFIT

Among the 361,662 men seen at the initial screening visit in the MRFIT, 133,117 (37%) reported smoking an average of 26 cigarettes per day. Mortality results for men screened were consistent with results from studies reported in the 1960s—significant associations between cigarette smoking and major causes of death were evident (Table 1). Smoking remained a powerful risk factor for cancers of the lung, pancreas, mouth, larynx, esophagus, kidney, and bladder and for total cancer deaths, as well as for CHD, stroke, and total mortality. Risks for smokers relative to nonsmokers ranged from greater than 6 for cancers of the lung, mouth, and larynx to 2–2.5 for other causes of death (Table 1). Overall, cigarette smoking was associated with 1,776 excess deaths from CHD and 4,856 excess deaths from all causes (50.5% of all deaths among cigarette smokers). These risk estimates associated with cigarette smoking are probably conservative since, based on the initial screen data, former smokers cannot be separated from those who never smoked cigarettes. It is also not known how many non-cigarette smokers smoked pipes, cigars, or cigarillos.

#### Randomized Participants

At screen 1, approximately 64% of the 12,866 randomized participants reported smoking an average of 33 cigarettes per day. Approximately 20% of participants

TABLE 1  
TEN-YEAR AGE-ADJUSTED MORTALITY RATES (PER 10,000 MEN) BY REPORTED CIGARETTE SMOKING STATUS FOR MEN SCREENED IN THE MRFIT

Endpoint (ICD-9 codes)	Cigarettes/day										Coefficient for cigarettes/ day <sup>d</sup>
	Nonsmokers <sup>a</sup> (n = 228,545)	1–15 (n = 27,838)	16–25 (n = 44,840)	26–35 (n = 28,730)	36–45 (n = 23,396)	46 (n = 8,291)	Adjusted relative risk †smoker/ nonsmoker <sup>b</sup>	Rate per 10,000	No. deaths	Rate per 10,000	
All-cause mortality	8,426	1,493	3,127	2,751	1,999	742	2.2*	950.1	742	950.1	0.0233*
CHD (410–414, 429.9)	2,973	537	1,157	832	629	239	2.3*	305.8	239	305.8	0.0228*
Stroke (430–438)	262	59	119	84	57	17	2.5*	20.9	17	20.9	0.0231*
All cancers (140–239)	2,690	423	1,029	761	751	285	2.4*	370.3	285	370.3	0.0258*
Lung (162)	456	130	479	371	411	157	6.7*	205.1	157	205.1	0.0469*
Pancreas (157)	172	24	69	40	35	9	2.0*	10.5	9	10.5	0.0198*
Mouth and Larynx (140–149, 161)	35	9	30	24	39	16	6.6*	21.1	16	21.1	0.0500*
Esophagus (150)	73	15	29	17	18	12	15.9	8.2	12	15.9	0.0289*
Kidney (189)	113	4.1	30	34	23	8	10.1	4.6	8	10.1	0.0225*
Bladder (188)	39	1.8	13	12	9	3	3.6	3.6	3	3.6	0.0247*

\* Includes exsmokers at first screen.

<sup>b</sup> Adjusted for age, diastolic blood pressure, serum cholesterol level, and race (black/nonblack).

<sup>c</sup> Regression coefficient for cigarettes/day in a proportional hazards model, with age, diastolic blood pressure, serum cholesterol level, and race (black/nonblack) in the model. The coefficients for cigarettes/day are all significant at the 0.0001 level.

\*\*  $P < 0.0001$ .

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TABLE 3  
NUMBER OF DEATHS (AND PERCENTAGE OF NUMBER RANDOMIZED) BY CAUSE FOR MRFIT SI AND UC PARTICIPANTS AT 10.5 YEARS OF FOLLOW-UP BY REPORTED SCREEN 3 SMOKING STATUS

Cause of death	ICD-9 code	Never smoked cigarettes			Exsmokers			Smokers		
		SI (n = 931)	UC (n = 928)	% difference <sup>a</sup>	SI (n = 1394)	UC (n = 1419)	% difference <sup>a</sup>	SI (n = 4103)	UC (n = 4091)	% difference <sup>a</sup>
All cardiovascular	390-459	31 (3.33)	31 (3.34)	-0.7	38 (2.73)	52 (3.66)	-25.8	197 (4.80)	207 (5.06)	-5.3
CHD	410-414, 429.2 <sup>b</sup>	23 (2.47)	21 (2.26)	11.2	33 (2.37)	40 (2.82)	-17.2	146 (3.56)	165 (4.03)	-11.7
Cerebrovascular	430-438	4 (0.43)	5 (0.54)	—	3 (0.22)	4 (0.28)	—	13 (0.32)	14 (0.34)	-5.9
Other CVD		4 (0.43)	5 (0.54)	—	2 (0.14)	8 (0.56)	—	38 (0.93)	28 (0.68)	32.2
All noncardiovascular		23 (2.47)	17 (1.83)	37.2	35 (2.51)	38 (2.68)	-2.5	171 (4.17)	191 (4.67)	-11.4
Neoplastic	140-239	10 (1.07)	9 (0.97)	—	23 (1.65)	23 (1.62)	6.1	107 (2.61)	117 (2.86)	-9.4
Respiratory and intrathoracic organs	160-165	0 (0.00)	0 (0.00)	—	9 (0.65)	4 (0.28)	—	57 (1.39)	51 (1.25)	11.2
Lung	162	0 (0.00)	0 (0.00)	—	9 (0.65)	4 (0.28)	—	56 (1.36)	50 (1.22)	11.6
Other neoplasms		10 (1.07)	9 (0.97)	—	14 (1.00)	19 (1.34)	-21.1	50 (1.22)	66 (1.61)	-25.3
Respiratory	460-519	4 (0.43)	1 (0.11)	—	1 (0.07)	3 (0.21)	—	8 (0.19)	12 (0.29)	—
Digestive system	520-579	4 (0.43)	2 (0.22)	—	2 (0.14)	3 (0.21)	—	16 (0.39)	11 (0.27)	46.0
Accidents, suicides, homicides	800-999	5 (0.54)	4 (0.43)	—	6 (0.43)	7 (0.49)	—	27 (0.66)	32 (0.78)	-17.0
Other non-CVD		0 (0.00)	1 (0.11)	—	3 (0.22)	2 (0.14)	—	13 (0.32)	19 (0.46)	-32.5
Cause unknown (death certificate not found)		0 (0.00)	0 (0.00)	—	0 (0.00)	0 (0.00)	—	1 (0.02)	1 (0.02)	—
Total		54 (5.80)	48 (5.17)	12.6	73 (5.24)	90 (6.34)	-16.1	369 (8.99)	399 (9.75)	-8.2

Note. ICD, International Classification of Diseases; SI, special intervention; UC, usual care; CVD, cardiovascular disease; CHD, coronary heart disease. Dashes signify less than 10 deaths in SI or UC groups; therefore, the percentage difference is not displayed.

<sup>a</sup> Defined as  $(RR-1) \times 100\%$ . RR estimated from proportional hazards regression model. None of the differences are significant at the 0.05 level.

<sup>b</sup> Cardiovascular disease, unspecified with use of Ninth Revision, coded as 412.4 with use of Eighth Revision.

TABLE 4  
RELATIONSHIP BETWEEN NUMBER OF CIGARETTES SMOKED AT SCREEN 1 AND CHD, LUNG CANCER, AND TOTAL MORTALITY AT 10.5 YEARS OF FOLLOW-UP FOR MRFIT PARTICIPANTS

	Number of participants	CHD			Lung cancer			Total mortality		
		Number of deaths	Adjusted RR <sup>a</sup>	95% CI	Number of deaths	Adjusted RR	95% CI	Number of deaths	Adjusted RR	95% CI
Never smoked cigarettes	1,859	44 (2.22) <sup>b</sup>	1.00	—	0 (0.00)	1.00	—	102 (5.13)	1.00	—
Exsmoker	2,813	73 (2.44)			13 (0.43)			163 (5.44)		
Smoker										
1-25	2,572	102 (3.80)	2.18	(1.66, 2.88)	19 (0.71)	3.11	(1.51, 6.41)	211 (7.87)	1.84	(1.52, 2.21)
≥26	5,622	209 (3.58)	2.58	(1.98, 3.35)	87 (1.49)	7.18	(3.76, 13.70)	537 (9.54)	2.70	(2.28, 3.21)
Regression coefficient (SE) for cigarettes/day in proportional hazards model (smokers only) <sup>c</sup>			0.0027 (0.0042)			0.0265 (0.0066)			0.0114 (0.0026)	
P-value			0.52			<0.001			<0.001	

<sup>a</sup> Adjusted for age, serum cholesterol, and diastolic blood pressure.

<sup>b</sup> Rate per 1,000 person-years.

TABLE 5  
RELATIONSHIP BETWEEN SERUM THIOCYANATE AND CHD, LUNG CANCER, AND TOTAL MORTALITY AT 10.5 YEARS OF FOLLOW-UP  
FOR MRFIT SCREEN 1 SMOKERS

	Number of participants	CHD			Lung cancer			Total mortality		
		Number of deaths	Adjusted RR <sup>a</sup>	95% CI	Number of deaths	Adjusted RR	95% CI	Number of deaths	Adjusted RR	95% CI
Quintile of thiocyanate (μmol/liter)										
<122	1,591	41 (2.45) <sup>b</sup>	1.00	—	15 (0.90)	1.00	—	105 (6.29)	1.00	—
123-156	1,578	63 (3.87)	2.21	(1.63, 2.99)	24 (1.48)	3.05	(1.74, 5.34)	155 (9.53)	2.04	(1.68, 2.47)
157-183	1,555	77 (4.76)	2.82	(2.12, 3.75)	10 (0.62)	1.32	(0.63, 2.75)	147 (9.09)	2.02	(1.66, 2.47)
184-213	1,630	63 (3.74)	2.30	(1.69, 3.13)	29 (1.72)	3.64	(2.11, 6.28)	159 (9.43)	2.13	(1.75, 2.59)
≥214	1,591	59 (3.60)	2.24	(1.64, 3.07)	24 (1.47)	3.34	(1.88, 5.92)	177 (10.81)	2.50	(2.07, 3.03)
Regression coefficient (SE) for thiocyanate in proportional hazards model <sup>a</sup>			0.0025 (0.0010)			0.0037 (0.0017)			0.0033 (0.0006)	
P-value			0.01			0.03			<.001	

<sup>a</sup> Adjusted for age, serum cholesterol, and diastolic blood pressure.

<sup>b</sup> Rate per 1,000 person-years.

TABLE 6  
RELATIONSHIP BETWEEN INITIAL AGE OF DAILY CIGARETTE SMOKING AND CHD, LUNG CANCER, AND TOTAL MORTALITY AT 10.5 YEARS OF FOLLOW-UP FOR MRFIT SCREEN 1 SMOKERS

	Number of participants	CHD			Lung cancer			Total mortality <sup>a</sup>		
		Number of deaths	Adjusted RR <sup>a</sup>	95% CI	Number of deaths	Adjusted RR	95% CI	Number of deaths	Adjusted RR <sup>a</sup>	95% CI
Age at screening 35-44										
Age began smoking										
≤15	978	25 (2.42) <sup>b</sup>	1.00	—	3 (0.29)	1.00	—	67 (6.49)	1.00	—
16-17	1,018	31 (2.89)	1.15	(0.67, 1.95)	8 (0.75)	2.81	(0.73, 10.78)	70 (6.52)	0.99	(0.70, 1.38)
18-19	753	16 (2.01)	0.77	(0.41, 1.46)	4 (0.50)	2.04	(0.44, 9.47)	39 (4.90)	0.74	(0.50, 1.11)
20-21	401	14 (3.28)	1.27	(0.66, 2.47)	0 (0.00)	N/A	N/A	20 (4.69)	0.70	(0.42, 1.16)
22-23	167	1 (0.57)	0.21	(0.03, 1.55)	0 (0.00)	N/A	N/A	10 (5.74)	0.85	(0.44, 1.67)
≥24	185	3 (1.52)	0.53	(0.16, 1.78)	0 (0.00)	N/A	N/A	6 (3.04)	0.45	(0.19, 1.04)
Regression coefficient (SE) for initial age of daily smoking in proportional hazards model <sup>a</sup>			-0.0277 (0.0305)			-0.0602 (0.0798)			-0.0381 (0.0204)	
P-value			0.36			0.45			0.06	
Age at screening 45-57										
Age began smoking										
≤15	1,087	54 (4.86)	1.00	—	22 (1.98)	1.00	—	135 (12.16)	1.00	—
16-17	1,224	51 (4.08)	0.82	(0.56, 1.20)	32 (2.56)	1.36	(0.79, 2.35)	153 (12.23)	1.01	(0.80, 1.27)
18-19	1,123	50 (4.30)	0.83	(0.56, 1.22)	21 (1.80)	0.97	(0.53, 1.76)	114 (9.80)	0.80	(0.62, 1.02)
20-21	628	37 (5.76)	1.11	(0.73, 1.69)	7 (1.09)	0.57	(0.24, 1.34)	82 (12.77)	1.02	(0.77, 1.34)
22-23	235	11 (4.55)	0.85	(0.44, 1.63)	6 (2.48)	1.31	(0.53, 3.24)	27 (11.16)	0.89	(0.58, 1.34)
≥24	359	17 (4.60)	0.88	(0.51, 1.53)	3 (0.81)	0.42	(0.13, 1.44)	42 (11.37)	0.90	(0.64, 1.28)
Regression coefficient (SE) P-value for initial age of daily smoking in proportional hazards model <sup>a</sup>			-0.0034 (0.0159)			-0.0279 (0.0268)			-0.0028 (0.0100)	
P-value			0.83			0.30			0.79	

<sup>a</sup> Adjusted for age, serum cholesterol, diastolic blood pressure, and cigarettes/day.

<sup>b</sup> Rate per 1,000 person-years.

TABLE 7  
RELATIONSHIP BETWEEN CIGARETTE NICOTINE CONTENT AND CHD, LUNG CANCER, AND TOTAL MORTALITY AT 10.5 YEARS OF FOLLOW-UP  
FOR MRFIT SCREEN 1 SMOKERS

	Number of participants	CHD			Lung cancer			Total mortality		
		Number of deaths	Adjusted RR <sup>a</sup>	95% CI	Number of deaths	Adjusted RR	95% CI	Number of deaths	Adjusted RR	95% CI
Nicotine (mg)										
≤1.0	1,777	68 (3.67) <sup>b</sup>	1.00	—	20 (1.08)	1.00	—	156 (8.42)	1.00	—
1.1-1.4	4,363	160 (3.52)	1.04	(0.80, 1.35)	51 (1.12)	0.97	(0.62, 1.52)	394 (8.68)	1.05	(0.89, 1.24)
≥1.5	1,319	60 (4.41)	1.27	(0.92, 1.77)	24 (1.76)	1.46	(0.85, 2.49)	157 (11.53)	1.36	(1.11, 1.67)
Regression coefficient (SE) for nicotine in proportional hazards model <sup>a</sup>			0.0294 (0.2046)			0.4142 (0.3648)			0.2517 (0.1328)	
P-value			0.89			0.26			0.06	

<sup>a</sup> Adjusted for age, serum cholesterol, diastolic blood pressure, and cigarettes/day.

<sup>b</sup> Rate per 1,000 person-years.

TABLE 8  
RELATIONSHIP BETWEEN CIGARETTE TAR CONTENT AND CHD, LUNG CANCER, AND TOTAL MORTALITY AT 10.5 YEARS OF  
FOLLOW-UP FOR MRFIT SCREEN 1 SMOKERS

	Number of participants	CHD			Lung cancer			Total mortality		
		Number of deaths	Adjusted RR <sup>a</sup>	95% CI	Number of deaths	Adjusted RR	95% CI	Number of deaths	Adjusted RR	95% CI
Tar (mg)										
≤15	992	39 (3.77) <sup>b</sup>	1.00	—	12 (1.16)	1.00	—	91 (8.79)	1.00	—
16-19	4,347	160 (3.54)	1.08	(0.80, 1.45)	48 (1.06)	0.81	(0.49, 1.33)	384 (8.49)	1.01	(0.83, 1.22)
≥20	2,120	89 (4.06)	1.19	(0.86, 1.65)	35 (1.60)	1.14	(0.67, 1.94)	232 (10.58)	1.21	(0.98, 1.49)
Regression coefficient (SE) for tar in proportional hazards model <sup>a</sup>			0.0089 (0.0128)			0.0227 (0.0223)			0.0179 (0.0082)	
P-value			0.49			0.31			0.03	

<sup>a</sup> Adjusted for age, serum cholesterol, diastolic blood pressure, and cigarettes/day.

<sup>b</sup> Rate per 1,000 person-years.

### Smoking Cessation among Randomized Participants

Smoking cessation in the MRFIT was assessed by self-report validated by the serum SCN level and, later, by expired air carbon monoxide levels (at the 36- and 72-month visits). Quitters were defined as screen 1 smokers, who at the 12-month visit reported not smoking and whose level of serum SCN was below 100  $\mu\text{mol/liter}$ . This definition is consistent with mortality results presented in an earlier report (5).

Both the SI and the UC smokers who stopped smoking during the first 12 months of the trial had lower CHD and total mortality rates than those who continued to smoke (Table 9) (24). There is no evidence of a reduction in lung cancer mortality associated with smoking cessation over this 10-year follow-up period. Most of the lung cancers, however, occurred among the heavier smokers, the group with the lowest cessation rates.

### DISCUSSION

The MRFIT results demonstrate that the risk of cancer and CHD mortality is substantially increased among smokers compared with nonsmokers and that this risk increases with the number of cigarettes smoked. These findings are consistent with those from the early longitudinal studies of the 1960s and early 1970s (11).

The MRFIT began in 1972 in a climate of increasing interest in risk factor interventions, including smoking cessation. Of the three clinical trials on the effect of smoking cessation on mortality which have been conducted (5, 25, 26), the

TABLE 9  
CHD, LUNG CANCER, AND TOTAL MORTALITY FROM THE END OF THE TRIAL THROUGH 12/31/85  
BY CIGARETTE SMOKING STATUS AT 72 AND 12 MONTHS FOR MRFIT SI AND  
UC SCREEN 1 CIGARETTE SMOKERS

	CHD			Lung cancer		All causes	
	No. men	No. deaths	Rate deaths	No. deaths	Rate deaths	No. deaths	Rate deaths
Special intervention							
Reported smoking cigarettes at 72 months							
Yes	1,810	40	5.91	14	2.07	95	14.03
No	1,734	20	3.04	9	1.37	49	7.45
Reported smoking cigarettes at 12 months							
Yes	564	7	3.28	1	0.47	17	7.96
No	1,170	13	2.93	8	1.80	32	7.21
Usual care							
Reported smoking cigarettes at 72 months							
Yes	2,488	59	6.35	14	1.51	142	15.27
No	1,009	16	4.20	6	1.58	38	9.98
Reported smoking cigarettes at 12 months							
Yes	686	13	5.04	3	1.16	27	10.46
No	323	3	2.44	3	2.44	11	8.96

MRFIT has been the largest. At the inception of the MRFIT, and throughout its duration, both England and the United States witnessed dramatic declines in the incidence of lung cancer. In the United States, the lung cancer rate per 100,000 white men age 35-44 years dropped from 15.4 in 1970 to 11.2 in 1980 to 9.4 in 1985 (27). Cardiovascular mortality also decreased in the United States (27).

The decline in the incidence of these diseases has been partially attributed to changes in smoking behavior (28). In the United States, two important changes have occurred in the last 30 years: The tar and nicotine content in cigarettes has decreased, and—particularly among the younger age groups—the percentage of individuals who smoke has substantially declined. For example, in 1965, 57.3% of 35-year-old white men smoked cigarettes, but by 1976, the percentage of smokers in this cohort had dropped to 46.8 and by 1985, had dropped further to 36.6 (1).

Although it is difficult to determine how much of the change in lung cancer and cardiovascular mortality in the United States has been due to modification of the cigarette, rather than the decline in the percentage of cigarette smokers, the results of the present study indicate that reduction in the tar and nicotine contents of cigarettes was unlikely to have had an important effect on mortality, since tar and nicotine contents were only weakly related to total mortality. Moreover, the duration of smoking as measured by the age of smoking onset was only weakly related to mortality. However, the duration of exposure to low tar/nicotine cigarettes was unknown. Participants may have switched to these types of cigarettes only after years of smoking higher tar/nicotine products.

The present study suggests that smoking cessation may be related to lower mortality rates from CHD. Individuals who quit smoking during the first year of the trial had a 37.2% lower CHD and 40.9% lower total mortality at 10.5 years than those who were still smoking at the end of one year (24). There was no evidence that smoking cessation resulted in a decrease in lung cancer mortality. This finding is consistent with the results from the large observational study of U.S. Veterans which noted that while risk of lung cancer declined with increasing length of time from initial smoking cessation, substantial excess risk, compared with veterans who never smoked, remained as long as 20 years after quitting smoking (29).

Lung cancer mortality in the MRFIT was more closely linked to dose as measured by the number of cigarettes smoked than was CHD mortality. The heavier smokers were less likely to stop smoking (30, 31). Almost all of the lung cancer deaths continued to occur among men who were heavy cigarette smokers (smoking 25 or more cigarettes per day) in the trial. The relatively low cessation rates among these high risk smokers may partially account for the failure to demonstrate any difference in lung cancer mortality. An irreversible cumulative effect of cigarette smoking exposure similar to radiation and other carcinogens may also be an important factor (28).

The smoking cessation rate for SI men was substantial and somewhat greater than anticipated during the trial (5, 18). However, the cessation rate among UC men was also higher than expected. By 72 months, the cessation rates among screen 1 smokers were 28.1 and 49.3% for UC and SI groups, respectively (30).

During the first year of the trial, when smoking cessation was the greatest, there was a 15.8% difference in the cessation rate between the SI and UC smokers (30).

The magnitude of the UC cessation rates and the lower than expected UC mortality rate reduced the power of the trial to detect significant differences between SI and UC men in CHD and total mortality. Based on epidemiological data, the 15.8% difference between SI and UC in 12-month cessation rates is estimated to result in a 6% decrease in both CHD and total mortality. After an average of 10.5 years of follow-up, mortality rates among all MRFIT men for CHD and all causes were lower for SI compared with UC men by 10.6 and 7.7%, respectively. Thus, the effects of smoking cessation may have accounted for much of the overall difference in CHD and total mortality between SI and UC participants. These differences due to smoking do not take into account changes in the dose of smoking or any reported smoking cessation after the first 12 months.

### CONCLUSION

In summary, the results of the MRFIT are consistent with other studies in demonstrating that compared with men who continue to smoke, men who stop smoking have substantially lower risks of both CHD and total mortality. The key question, therefore, is not whether smoking cessation is beneficial, but rather, whether it is possible to substantially increase the number of individuals who stop smoking and remain exsmokers, especially among the heavier smoking group. The results from this study point to the need for special emphasis on the latter group with regard to smoking cessation in order to reduce its high risk of CHD. This continues to be an important public health concern.

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## Association between Baseline Risk Factors, Cigarette Smoking, and CHD Mortality after 10.5 Years<sup>1</sup>

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**Methods.** The association between baseline risk factors and death from coronary heart disease (CHD) after 10.5 years was investigated for cigarette smokers and nonsmokers who entered the Multiple Risk Factor Intervention Trial (MRFIT).

**Results.** Rates per thousand person-years of CHD mortality were higher for smokers than for nonsmokers at every level of baseline risk factors examined. There were significant associations between CHD mortality and plasma low-density lipoprotein and high-density lipoprotein cholesterol for smokers and nonsmokers. The inverse association between CHD mortality and high-density lipoprotein cholesterol was significantly stronger among nonsmokers compared with that among smokers and was attributable to a very strong association for former smokers. An inverse relationship between CHD and body mass index was evident for smokers and nonsmokers. Rates of CHD death rose sharply when levels of fasting glucose exceeded 140 mg/dl, and there was a significant association between CHD mortality and blood sugar levels for nonsmokers but not for smokers. For both smokers and nonsmokers, an inverse univariate association between alcohol consumption and CHD mortality was evident. This association, however, did not persist after adjustment for plasma high-density lipoprotein cholesterol.

**Conclusion.** Intervention on blood pressure and blood lipids is particularly important among cigarette smokers because of their increased risk of CHD death. The different associations between high-density lipoprotein cholesterol, fasting serum glucose, and CHD mortality for smokers and nonsmokers requires further investigation.

### INTRODUCTION

The 12,866 participants randomized to the Multiple Risk Factor Intervention Trial (MRFIT) have been followed for an average of 10.5 years. Extensive information regarding risk factors for coronary heart disease (CHD) was collected from all participants upon entry into the trial. A previous report evaluated the association between baseline risk factors and mortality from CHD and all causes during the first 7 years of follow-up (1). This report found that levels of high-density lipoprotein cholesterol (HDL-C) and low-density lipoprotein cholesterol (LDL-C), blood pressure (BP), and cigarette smoking were strong predictors of CHD mortality. Cigarette smoking was also a strong predictor of all-cause mortality.

After 10.5 years, randomized MRFIT cigarette smokers were at increased risk of death from CHD, lung cancer, and all causes compared with nonsmokers (2).

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